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OPTIMISING NUTRITION IN CF ADULTS

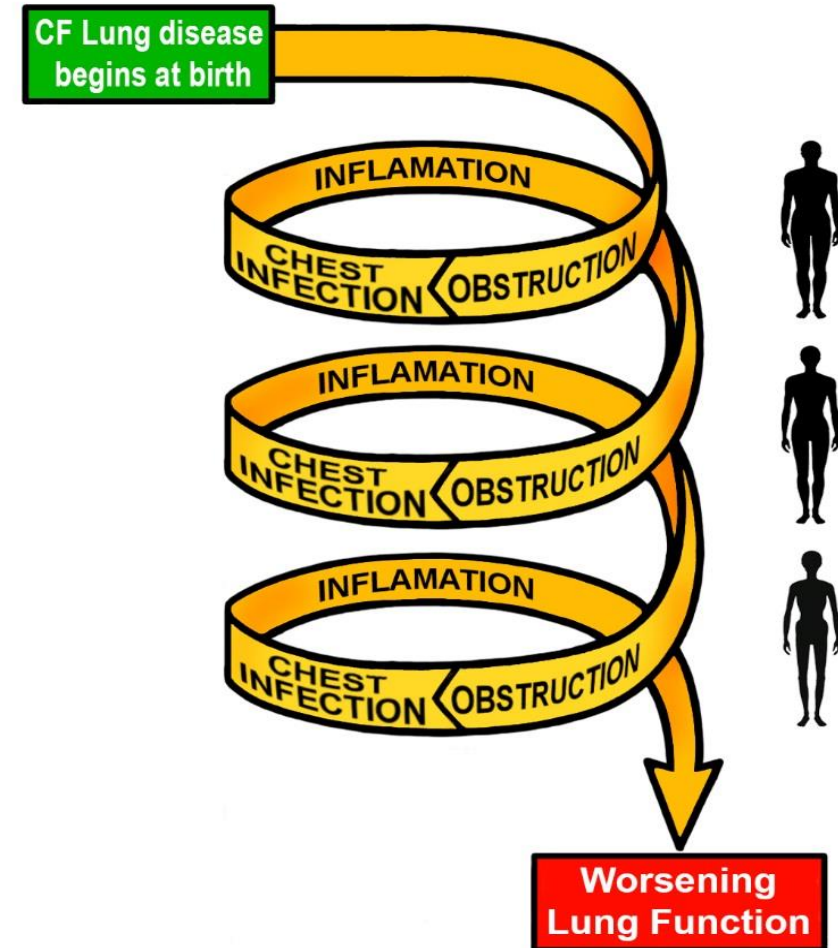
DR HELEN WHITE

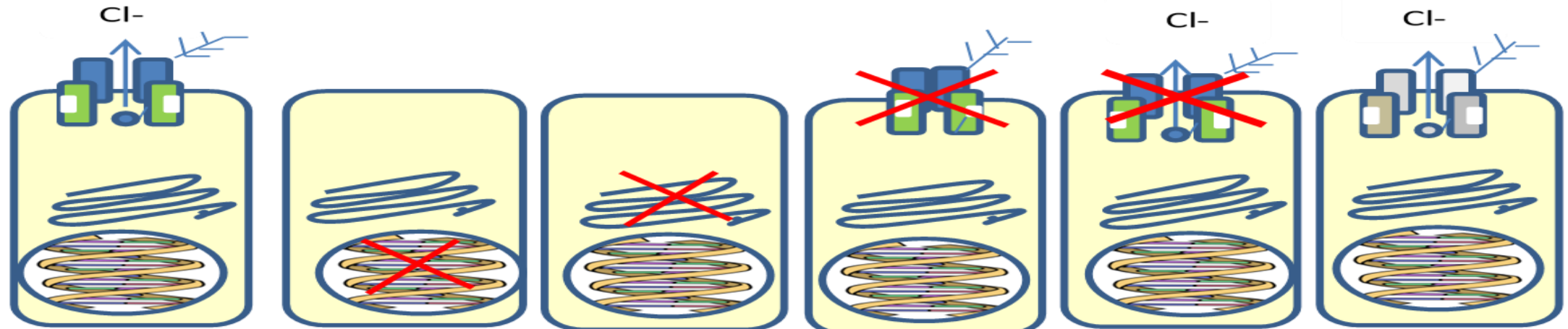


MULTISYSTEM DISEASE

Pancreatic insufficiency	Nutritional status CF related diabetes Fat soluble vitamin status Bone health
Increased requirements	Nutritional status
CFTR	Differing nutritional needs between Genotype
CF Related liver disease	
Pregnancy	
Transplantation ...	

Greater complexity of care in adulthood





Normal

Class I

Class II

Class III

Class IV

Class V

Class I mutations

CFTR production is stopped early and protein production becomes defective. Class 1 patients have no functioning CFTR chloride channels

Class II mutations

CFTR is poorly processed and is destroyed within the cell, resulting in little or no CFTR reaching the cell surface

Class III mutations

CFTR reaches the cell surface but does not work, unable to open properly to transport chloride

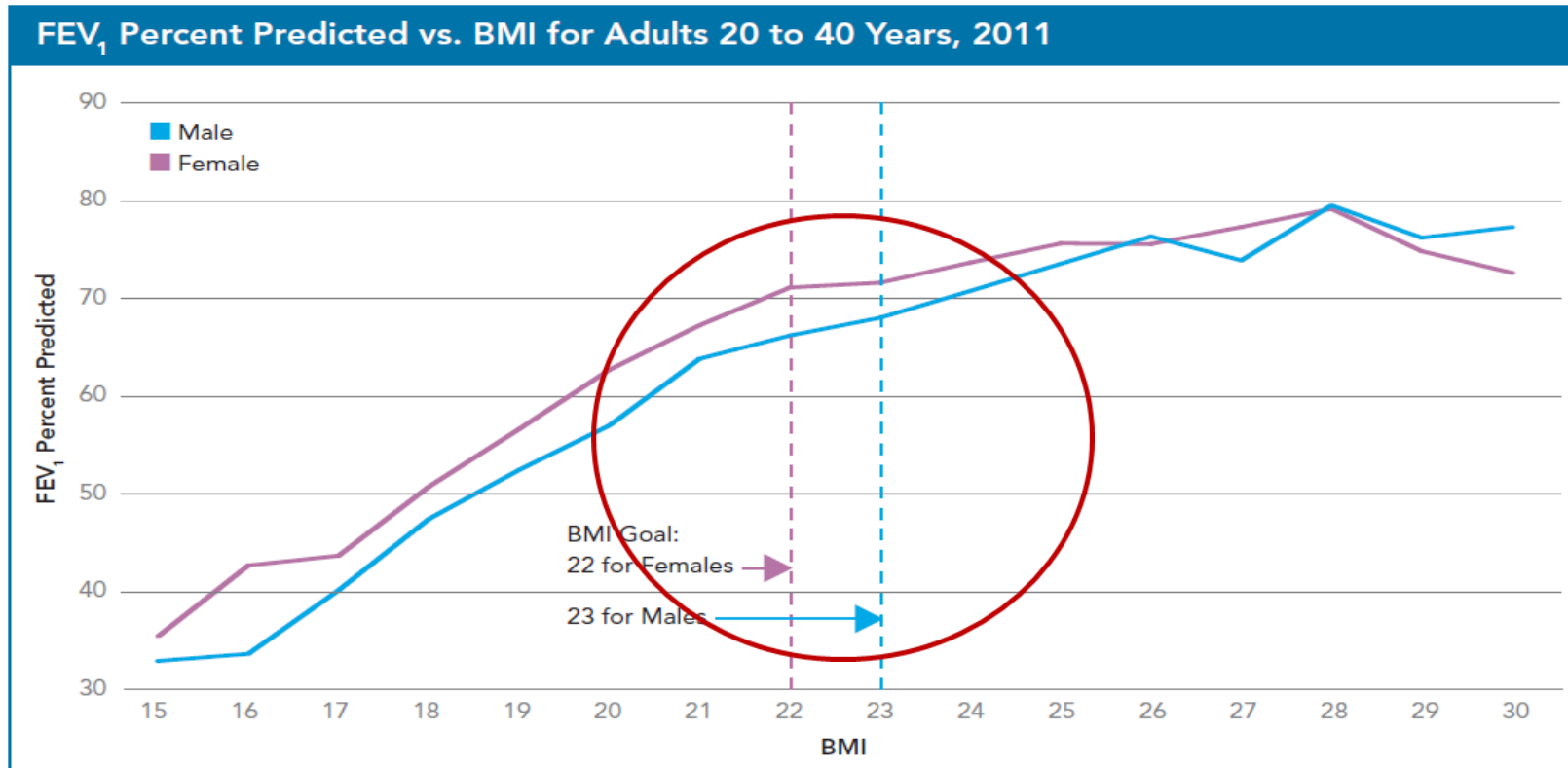
Class IV mutations

CFTR reaches the apical surface but the defective conduction of chloride through the channel results in poor CFTR function

Class V mutations

Decreased production of CFTR results in some production, but insufficient to maintain normal function

REASONS FOR NEW TARGETS?

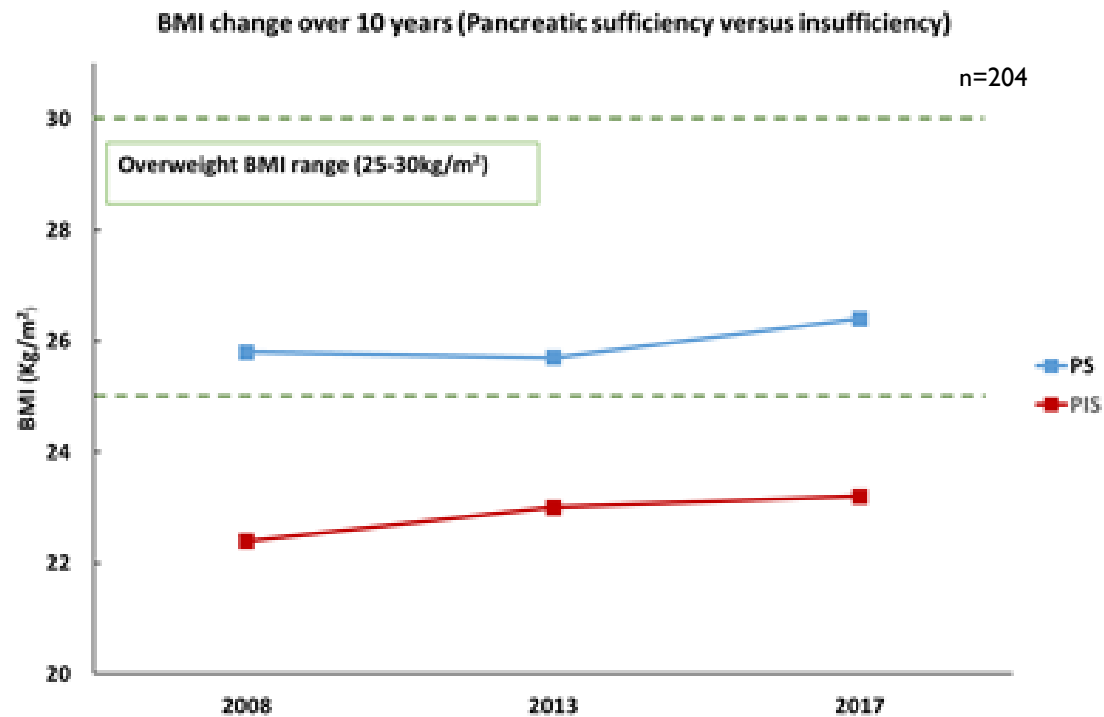


Lesser gains above BMI
22 (women), 23 (men)

Advantages reduce as
BMI reaches 30

Adults

LONGITUDINAL CHANGES IN BMI



N.J. Greig, H. White, H.K. Chadwick, A. Cartwright, D.G. Peckham
Cardiovascular risk in an adult CF population : a 9 year retrospective analysis

ENERGY & MACRONUTRIENT TARGETS

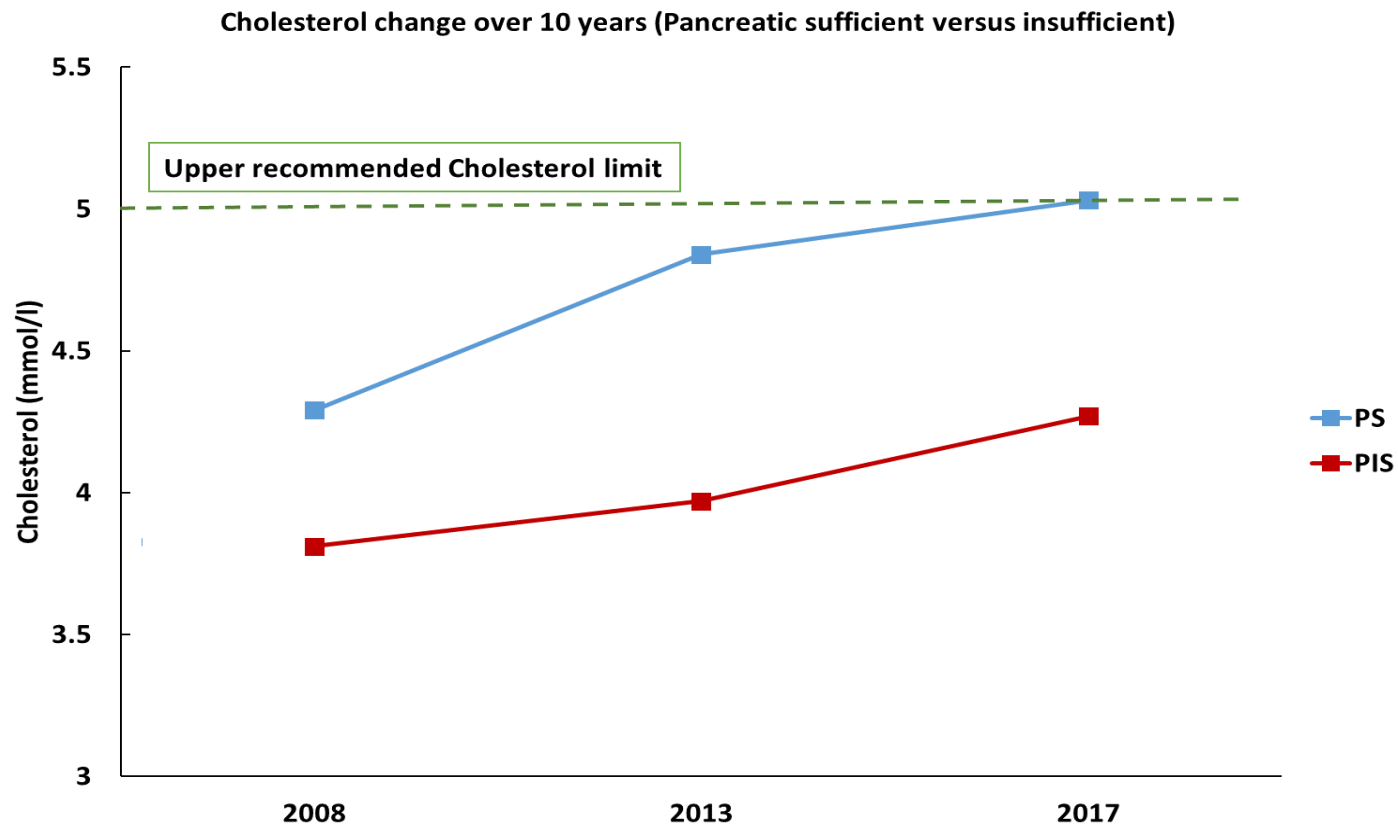
DIETARY EMPHASIS ON FATS



Fat 35-40% of
intake



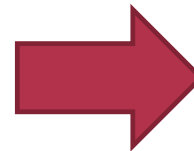
DIFFERING ADULT POPULATIONS



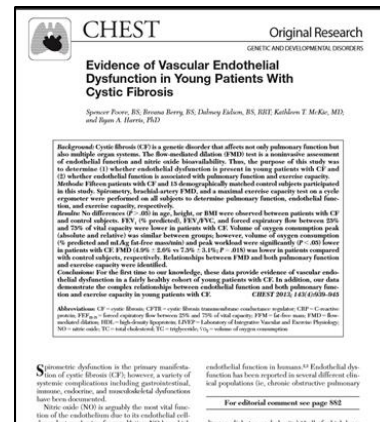
N.J. Greig, H. White, H.K. Chadwick, A. Cartwright, D.G. Peckham
Cardiovascular risk in an adult CF population : a 9 year retrospective analysis

WHAT TYPES OF FAT?

- Greater longevity
- Vascular endothelial dysfunction shown in children with CF (2013)
- Ischaemic heart disease reported in CF(2010)



- Greater emphasis on polyunsaturated and mono-unsaturated fats
- May also improve essential fatty acid status



- CF Trust (2016) &
- ESPEN-ESPGHAN-ECFS guidelines (2016)

HIGH PROTEIN....?



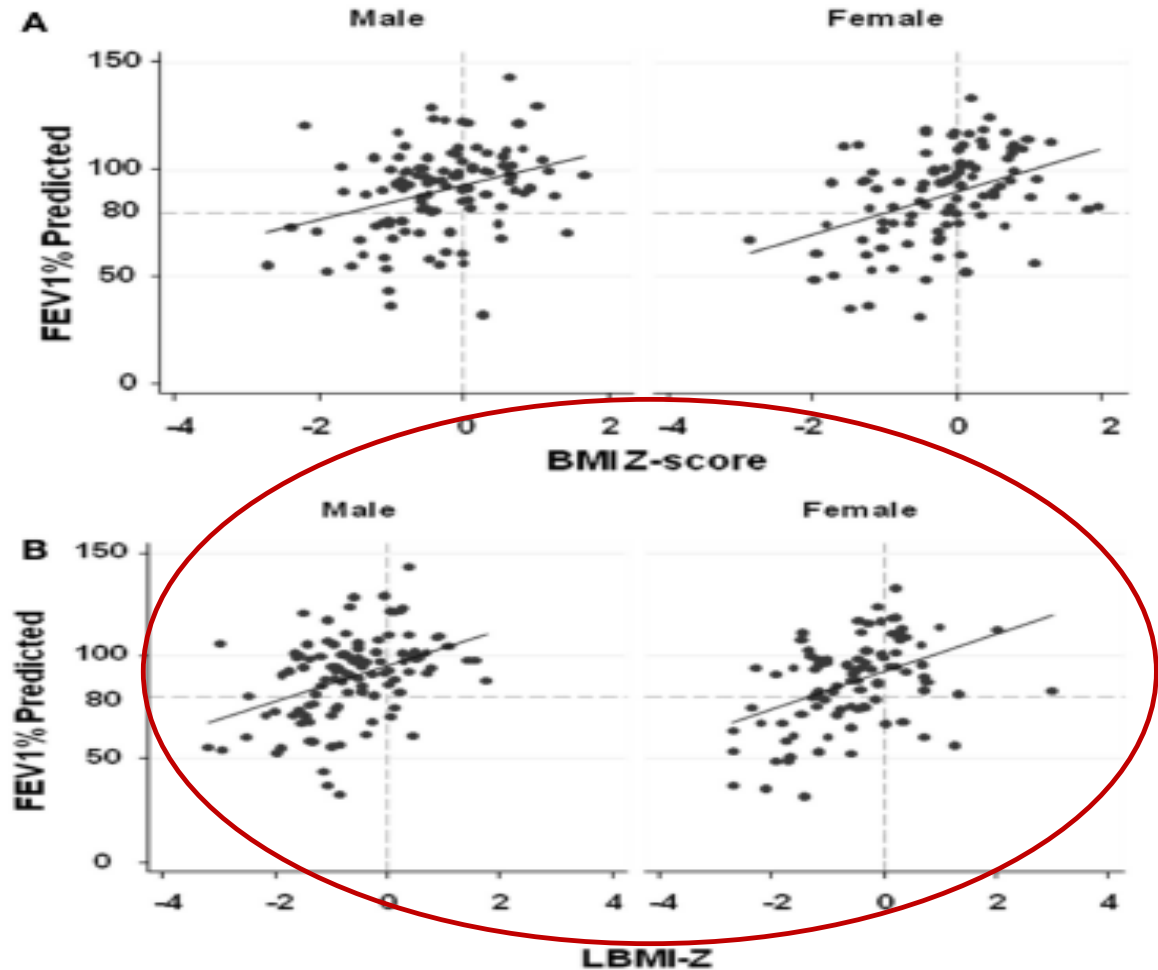
Protein

No evidence based recommendations for daily protein intake
for CF (CF Trust 2016)
20% energy ESPEN-ESPGHAN-ECFS (2016)
0.83g protein/kg

- Low muscle mass is consistently associated with pulmonary decline
- Protein digestion capacity is severely impaired in CF

SHEIKH ET AL, 2014

- High likelihood of normal lung function, targeting BMI z-score > 0
- Improved further, by targeting LBM z-score > 0



SUPPLEMENTS – WHICH ONES?



Complete
supplement – small
volume (125ml)



Complete
supplement – 200ml
volume

Fat free supplement
– no enzymes
required



High calorie, high fat
supplement (600kcal/240ml
drink)

ORAL CALORIE SUPPLEMENTS – COCHRANE REVIEW (2014)



■ Limited trials

■ Kalnins et al (2005)

- 21 %, 28% intake from oral calorie supplements at 1 and 3 months (mean 1.6 cans/day)
- No change in weight or height z-score

■ Hanning et al (2005)

- 25 % of EAR energy intake from supplements additional to normal diet
- No change in weight or height z-score at 6 months

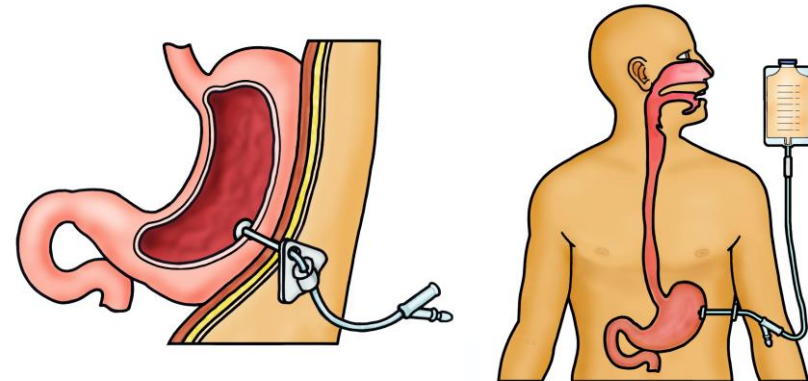
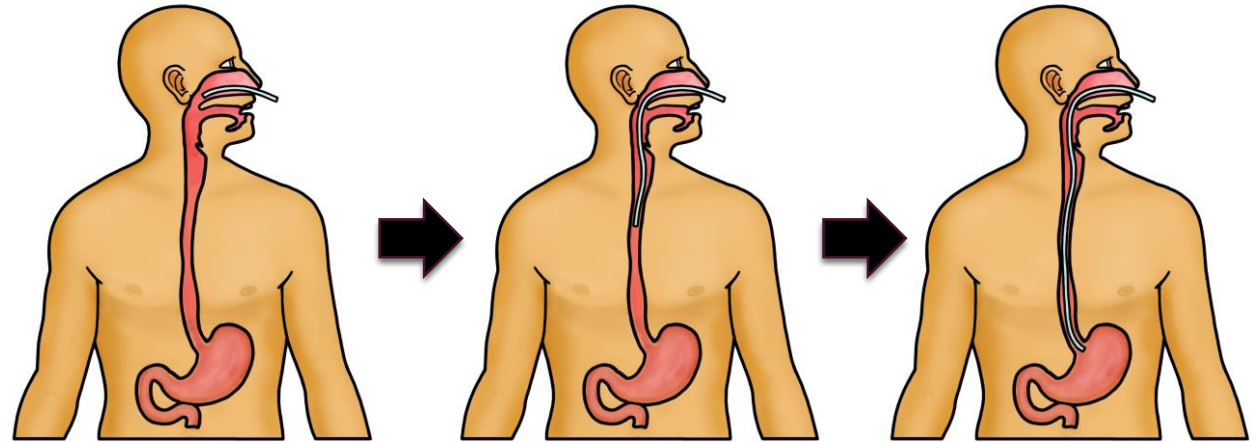
■ Poustie et al (2006) Oral protein energy supplements for children with cystic fibrosis: CALICO multicentre randomised controlled trial

- No improvements in children with cystic fibrosis who were moderately malnourished

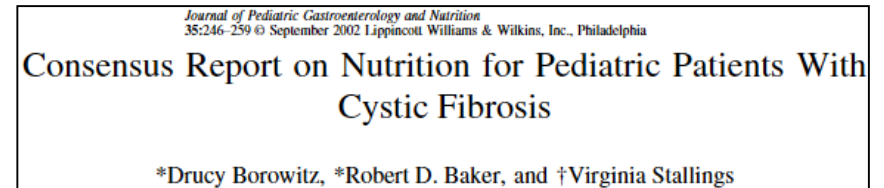
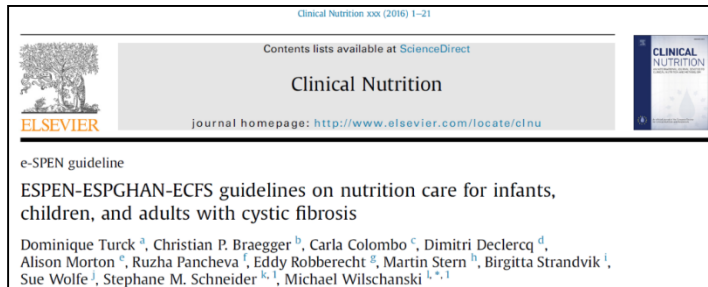


ENTERAL TUBE FEEDING FOR INDIVIDUALS WITH CF: CF FOUNDATION EVIDENCE INFORMED GUIDELINES (2016)

- ETF can improve age dependent anthropometrics
- ETF is given as a continuous overnight infusion
- Cannot recommend ETF to improve or stabilise lung function
- Recommends against FEV_1 being used as a contraindication to PEG or G-Tube placement



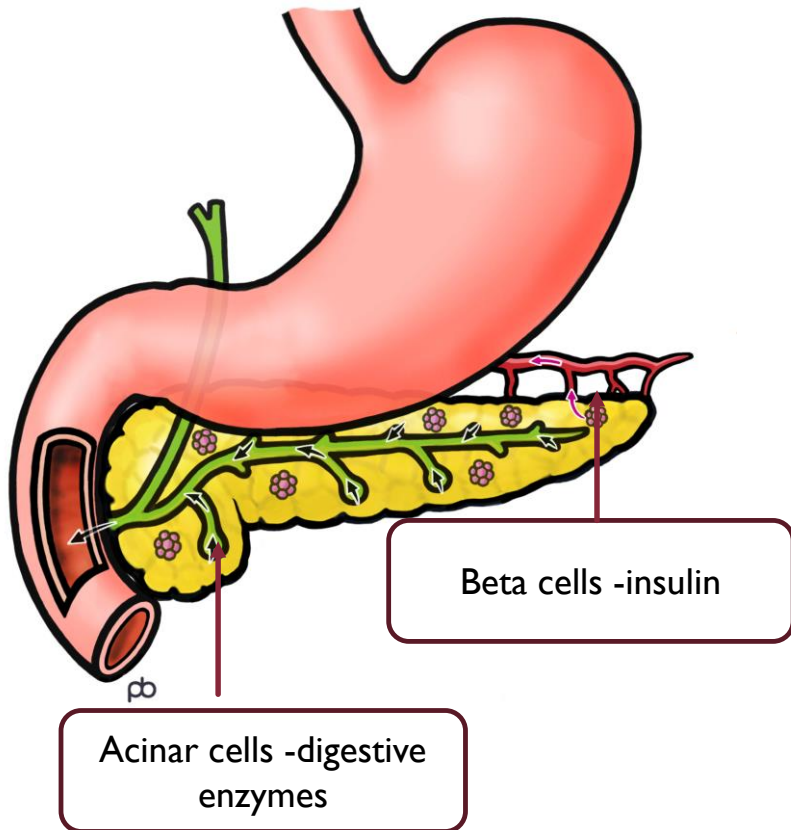
ENTERAL TUBE FEEDING - WHAT ARE THE LATEST KEY DOCUMENTS?



WHAT ELSE TO CONSIDER IN OPTIMISING NUTRITION

- High energy/high protein diet
- Oral dietary supplements
- Enteral tube feeding
- Enzyme therapy
- Vitamin supplementation (A,D,E,K)
- Co-morbidities – cystic fibrosis related diabetes, bone disease
- Pregnancy
- Transplantation
- New therapies

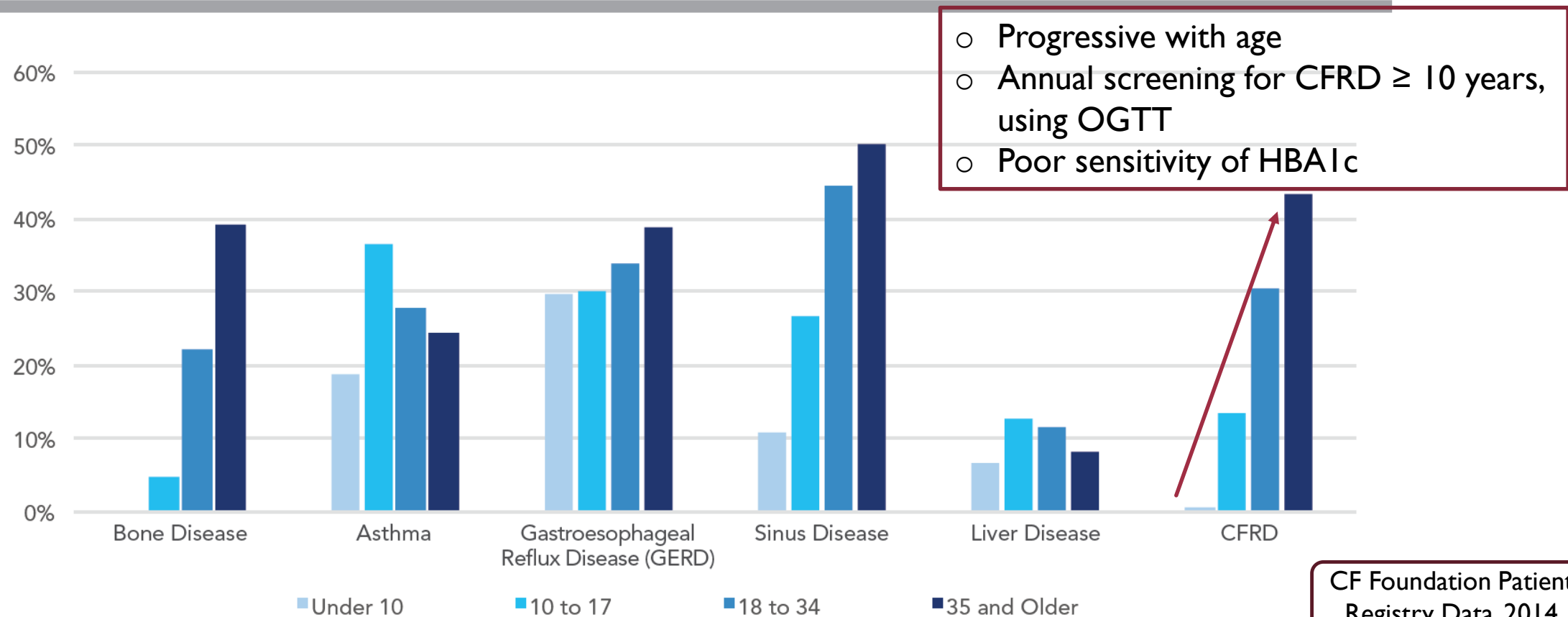
CYSTIC FIBROSIS RELATED DIABETES - THE BASIC DEFECT



- Pancreatic β cell dysfunction, fatty infiltration and fibrosis
- Causes decreased but not absolute insulin deficiency
- Diabetic ketoacidosis is rare
- Develops insidiously
- Patients may be asymptomatic
- Often first presents where insulin resistance is increased
 - Acute pulmonary infection
 - Chronic severe lung disease
 - Glucocorticoid therapy
 - Immunosuppression regimens (post-transplant)

AT WHAT STAGE DOES IT BEGIN TO OCCUR

Prevalence of Common Complications by Age in 2014



CYSTIC FIBROSIS RELATED DIABETES CHANGING FOCUS

Study	Cohort (n)	Findings for CFRD
Finkelstein et al, 1988	448	Increased mortality Worse nutritional status and lung function
Koch et al, 2001	7756	Worse nutritional status and lung function (greatest discrepancies at puberty)
Sims et al, 2005	2640	Worse pulmonary disease in females
Marshall et al, 2005	8247	Worse nutritional status, increased pulmonary exacerbations, increased liver disease
Adler et al, 2008	8029	Greater risk of CFRD in females Worse pulmonary function and liver function. CFTR class effect
Moran et al, 2009	872	Worse lung function (males) but Gender gap in mortality is narrowing No nutritional differences Pulmonary and nutritional differences do not differ by fasting glucose status

CRUCIAL CHANGES TO CARE

- Annual screening using the oral glucose tolerance test

Oral Glucose Tolerance Test

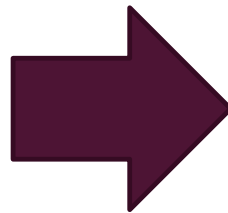


The pathologist will give you:
75 ml glucose drink

Then ask you to:
Wait 2 hours



Take blood
and test
glucose
levels

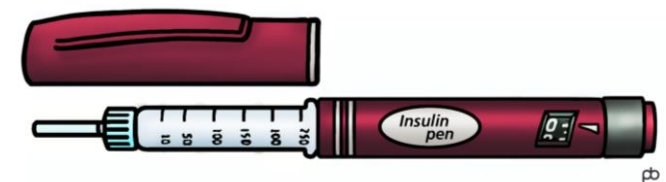
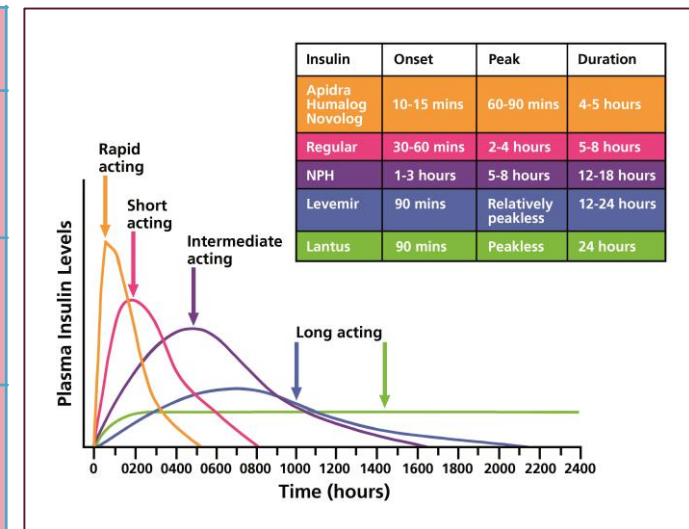


- Early instigation of insulin therapy



NUTRITIONAL GAINS ASSOCIATED WITH INSULIN TREATMENT

	3 months	6 months	1 year	2 year
Moran et al, (2009)			2% ↑ BMI	↑
White et al (2009)			3.3% ↑ BMI	5.9 % ↑ BMI
Nousia Avanitarkis et al, (2001)		16.6% ↑ BMI		
Rafii et al, (2005)	2.4% ↑ BMI	6.9% ↑ BMI		



DIETARY RECOMMENDATIONS ... CHANGE?

Update on cystic fibrosis related diabetes Kelly A, Moran A [Journal of Cystic fibrosis 2013;12;318-331]

- Consuming simple CHO in combination with complex CHO, protein and fat may limit the glucose excursion

CF Trust Nutritional management of Cystic Fibrosis (2016)

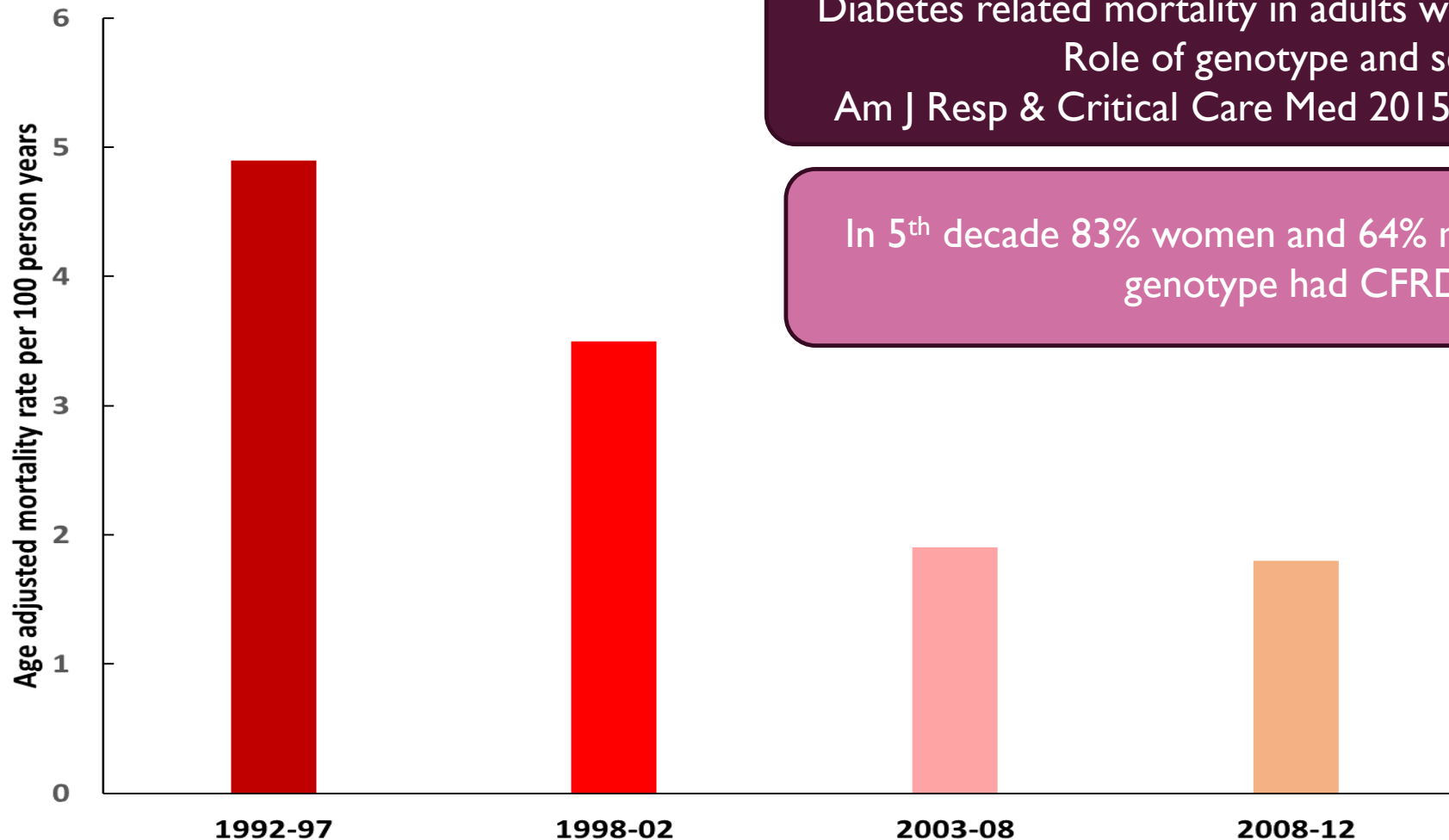
- Type I /II advice inappropriate
- Some people may be taught CHO counting
- If they do not CHO count regular meals should be encouraged containing complex CHO and limiting simple CHO to mealtimes



Insulin initiation and dose adjustments should be done conservatively
- to avoid hypoglycemia.

LEWIS ET AL (2015)

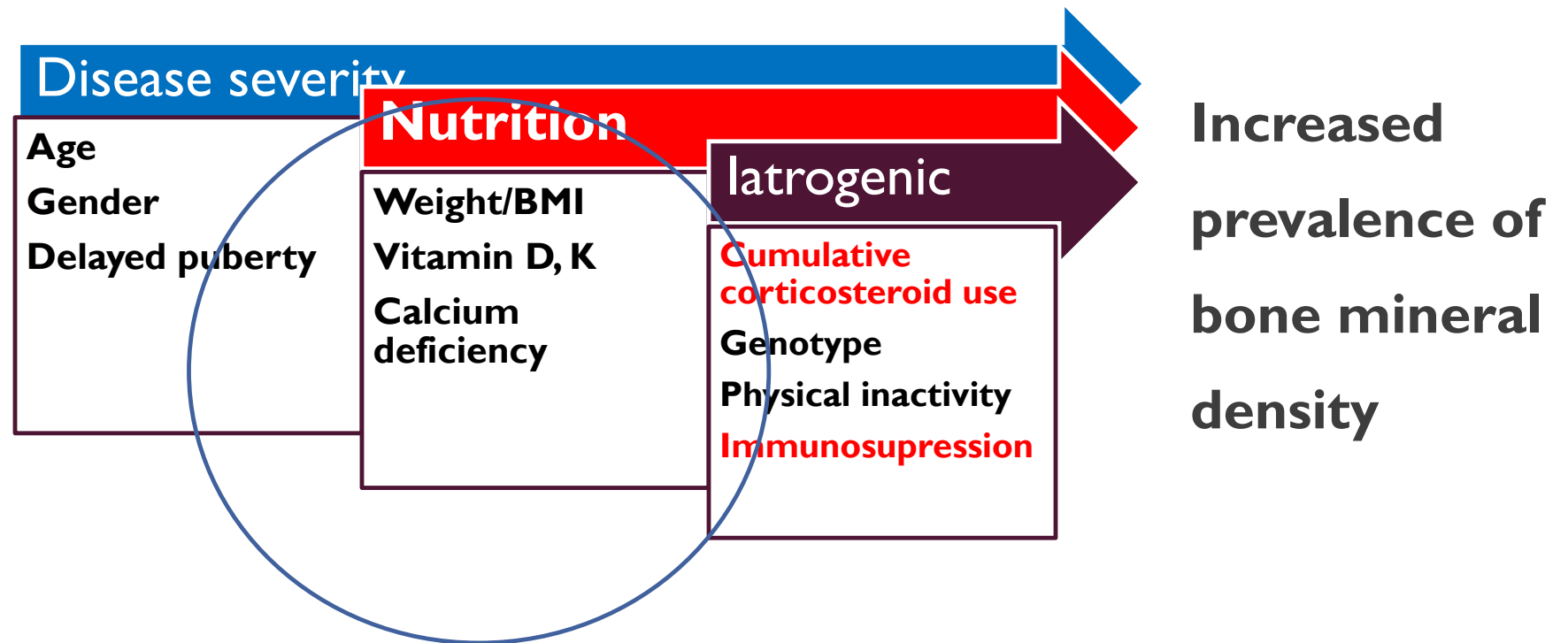
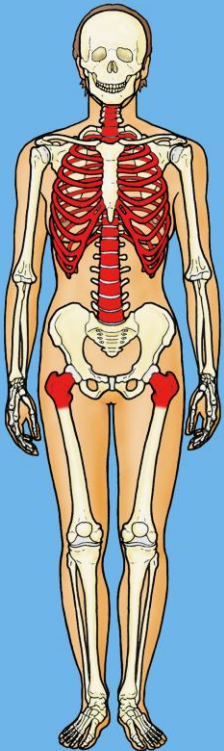
DIABETES – RELATED MORTALITY IN ADULTS WITH CYSTIC FIBROSIS



Diabetes related mortality in adults with cystic fibrosis:
Role of genotype and sex
Am J Resp & Critical Care Med 2015;191(2);194-200

In 5th decade 83% women and 64% men with a severe genotype had CFRD

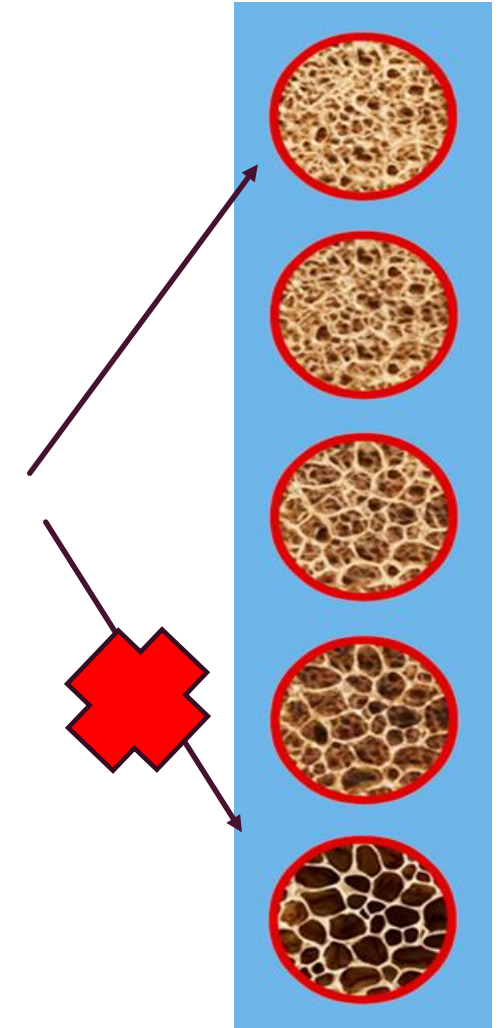
TREATMENT CONSIDERATIONS FOR PREVENTING LOW BONE MINERAL DENSITY



A NUTRITIONAL PROBLEM

Requirements for normal bone mineralisation

Adequate bone mass	(especially during the growth spurt)
Protein	osteoid formation
Vitamin D	Calcium absorption and phosphate utilisation
Calcium, phosphate and Magnesium	Bone calcification and mineralisation
Vitamin K	Carboxylation of osteocalcin



RISK FACTORS FOR VITAMIN D DEFICIENCY IN CF

- Reduced absorption *Lark et al, 2001*
- Inadequate supplementation
- Non adherence to therapy
- Reduced stores due to depleted fat mass
- Reduced sunlight exposure because of illness and medications
- Low vitamin D binding proteins *Speeckaert et al, 2008*
- Mg deficiency causes functional vitamin D deficiency (renal 25 OHD to 1,25(OH)₂D)

VITAMIN D INSUFFICIENCY PERSISTS IN CF

	Paediatric	Insufficiency/deficiency
Canada	Grey et al, 2008	88% insufficient
USA	Green et al 2008	46% insufficient
France	Sermet-Gaudelus et al, 2008	90% insufficient
UK	Conway et al., 2008	78% insufficient 15.0% deficient
Russia	Asherova et al, 2008	41.7% insufficient 16.6% deficient

TRENDS IN BMD STATUS

- Vitamin D intakes had increased by 53%
- Contributing factors may include steroid use, low BMI, inadequate calcium and vitamin D intake, and poor nutrient absorption, as well as effects of gene mutation on bone cells



Journal of Cystic Fibrosis 14 (2015) 528–532



Original Article

Trends in bone mineral density in young adults with cystic fibrosis over a 15 year period☆



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Received 24 June 2014; revised 11 December 2014; accepted 30 January 2015

Available online 16 February 2015

VITAMIN D SUPPLEMENTATION

- > 1 years 1,000-5,000 IU Vitamin D₃/day

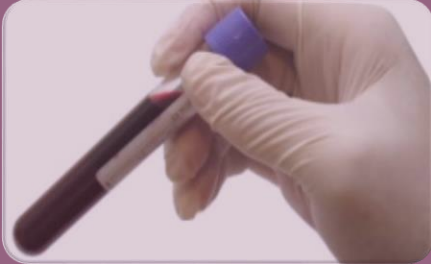
ECFS, 2011

- Aiming for minimum of 50nmol/L

CONTINUED DEBATE

- ① Target serum level >20 or >30ng/ml (50-75nmol/l) – mixed guidance
- ② Timing (Possible improved absorption with food and enzymes)
- ③ Vitamin D2 or Vitamin D3? - Vitamin D3 (Cholecalciferol)
- ④ Intervals (no evidence for bolus versus daily dosing)
- ⑤ UV lamps (no recommendation)

GREATER CERTAINTY...



Vit D measured by total serum 25(OH) D as it is associated with health outcomes, is the primary circulating form of Vit D and accounts for Vit D from diet & sunlight



Assess during the winter months (winter levels shown to be only 70% of summer values)



Repeat intervals following changes in treatment should be undertaken at 3 months

CALCIUM

- Should be assessed at least annually (ESPEN-ESPGHAN-ECFS Guidelines)
- Daily calcium intakes should be at a minimum to achieve dietary intake recommended by the EFSA



Calcium intake for people with CF:
recommendations guided by EFSA

Age	Dietary reference values
0-6 months	200mg
7-11 months	280mg
1-3 years	450mg
4-10 years	800mg
11-17 years	1150mg (1300mg 9-18yrs)
18-25 years	1000mg
>25 years	950mg

VITAMIN K

- Sub clinical as assessed by increased PIVKA II- almost universal in CF *Conway et al, 2005; Rashid et al, 1999; Becker et al, 1997; Wilson et al, 1997*
- Increased % of undercarboxylated osteocalcin (Glu-Oc) *Fewtrell et al, 2008; Grey et al, 2008; Nicolaidou et al, 2006; Conway et al, 2005; Aris et al, 2003*
- Associated with increased bone turnover
- Reduced markers of bone mineral accrual



European Guidelines – routine supplementation of all pancreatic insufficient patients
Infants 0.3-1mg/day
Older children and adults 1-10mg/day



UK (CF Trust, 2016)
routine supplementation of all pancreatic insufficient patients (phytomenadione)
Babies & infants <2 years 300µg/kg/d
2-7 yrs 5mg/day
> 7 yrs 5-10mg/day

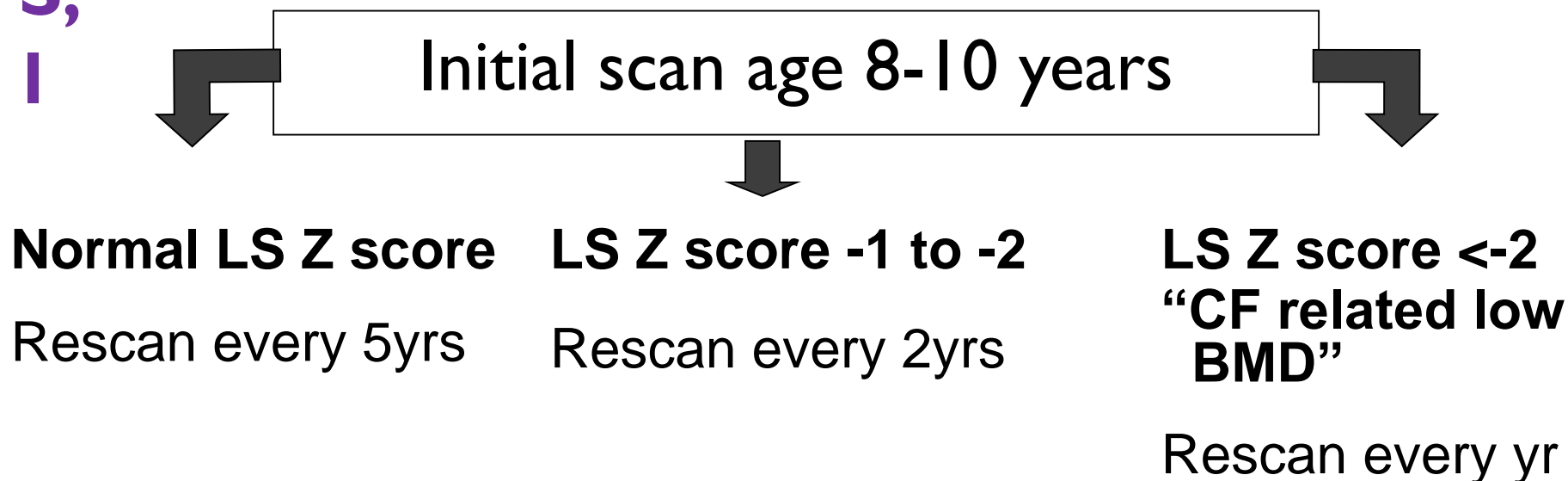
European Cystic Fibrosis Bone Mineralisation Guidelines

‘If height is ≥ 1 SD below age and sex matched healthy controls, BMD Z scores should be adjusted for height or statural age to avoid overestimating deficits in BMD in people with short stature’

Stress the importance of serial height adjusted measurements

Sermet-Gaudelus et al, 2011

**ECFS,
2011**



SUMMARY

- Greater complexity of nutritional management and emergence of new therapies
 - Diet, oral supplementation, enteral tube feeding
 - Pancreatic enzyme therapy introduction
 - Vitamin Supplementation (Vitamin A,D, E, K)
 - Cystic fibrosis related diabetes, osteoporosis, management of pregnancy, post-transplantation.... and others
- Improvements in nutritional status over the last 10 years aligned with earlier and more aggressive interventions across all aspects of nutritional management
-The future for our adult populations?